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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/660,052	09/10/2003	Laura C. Blumberg	PC10770B	7289

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PFIZER INC.
PATENT DEPARTMENT, MS8260-1611
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EXAMINER

BERNHARDT, EMILY B

ART UNIT PAPER NUMBER

1624

DATE MAILED: 06/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/660,052	Applicant(s) BLUMBERG ET AL.	
	Examiner Emily Bernhardt	Art Unit 1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 10,11 and 20-33 is/are pending in the application.
 4a) Of the above claim(s) 21 is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 10,11,20 and 22-33 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>12/15/03</u> . | 6) <input type="checkbox"/> Other: ____. |

Consistent with parent, restriction to one of the following inventions is required under 35 U.S.C. 121:

- I. Claims 10,11,20,22-33, drawn to compounds and compositions where R4=aryl, classified in class 544, subclasses such as 391,357,121 and many others as determined by nature of remaining substituents permitted thereon; class 514 subclass 255.01,235.8,etc.
- II. Claims 10,11,20,22-33, drawn to compounds, compositions where R4=heteroaryl, classified in class 544, subclasses such as 238 when pyridazine is R4, 235 when cinnoline is R4, 363 when R4=quinoline, and many other subclasses based on the exact nature of ring present as well as additional substituents thereon; class 514 subclasses various, namely from 247 and onward.
- III. Claims 10,11,21-33, drawn to compounds, compositions where R4=aryl, classified in class 544, subclasses such as 391 and others as may be determined by the nature of species exemplified; class 514 subclasses various.
- IV. Claims 10,11, 21-33, drawn to compounds, compositions where R4=heteroaryl, classified in class 544, subclasses various based on the exact nature of species exemplified.

In addition to an election of one of the above groups applicants must also elect a single species to which claims may be limited should generic claims be found not allowable.

The inventions are distinct, each from the other because of the following reasons: Compounds in I-IV are structurally dissimilar in view of the varying substitution permitted at all ring positions (but especially at R5 which is quite extensive) as well as linking groups connecting the piperazine ring to the R4 rings which can also vary. Such a scope in addition to varying classification would require separate online searches to accommodate the number of permutations such a scope would be expected to produce. Each can support a patent as the compounds are made and used independently of each other.

During a telephone conversation with Mr. Verni on 6/14/04 a provisional election was made with right of traverse to prosecute the invention of I (same election as in parent), and in particular species of eg.23, claims 10,11,20,22-33. Affirmation of this election must be made by applicant in replying to this Office action. Claim 21 is withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Claims which link various inventions will only be examined with respect to the elected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

The disclosure is objected to because of the following informalities: Parent history needs complete revision. See format suggested in MPEP 1302.04. Also status of most recent parent needs to be updated.

Appropriate correction is required.

The abstract of the disclosure is objected to because none of the variables “are as defined above” but rather as defined in the specification . Also an “are” should be inserted before “useful” on the last line. Correction is required. See MPEP 608.01(b).

Claims 10-11,20,22-33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. "Acetyl" wherever it appears in the complex moieties in the R5 definition and possibly elsewhere is defined in the specification to mean something that is not art-recognized for this well-known term and hence obscures intended scope. Note In re Hill 73 USPQ 482. Thus its not clear in the context which the term appears if C(O)CH₃ might be intended or the broader C(O)alkyl. If the latter the "special" definition for "acetyl" needs to be recited in the main claim. See claims 20,24,26,28,29 and 31.

2.Scope of "heterocycloalkyl","heteroaryl" in the many moieties recited for all R choices in the claims is unclear as to intended scope. Specification's definition is open-ended and thus non-limiting. Note the wording "etc." present at the end of both lists. Other than the rings particularly described in the specification it is not clear what other hetero atoms as ring members are intended . Note In re Wiggins 179 USPQ 421 regarding such terminology. A similar issue was present in Ex parte Remark 15 USPQ2d 1498 (at p.1500) in which it was decided that claim language that relied on open-ended language was "vague and uncertain" since it was not clear what else was intended to be covered.

3. In claim 33 there is a comma followed by "Other preferred compounds.... include" which is incorrect punctuation since a period should be present not a

comma but only 1 sentence is permitted per claim. The text that follows should simply be recited in the alternate as done for remaining R5 choices.

4. In main claim 20 there are several instances of “wherein R⁵ is” which appears superfluous since the text before it also pertains to R5 choices. See p.6 and 7.

5. Composition claims 10 and 11 are substantial duplicates. Note that intended uses in such claims is given no material weight. See *In re Tuominen* 213 USPQ 89 and MPEP 2111.02.

Claims 10-11,20,22-33 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. .

Specification does not adequately enable for the scope of elected piperazines claimed which can have a plethora of functional groups including a vast range of hetero-containing moieties throughout the R variables but especially at R5. Compounds made and some presumably tested for CCR1 antagonistic activity (however no indication which compounds were tested) fall far short of the claims’ scope as only 4-F benzyl derivatives are exemplified with H and/or Me as substituents on piperazino carbons. Substitution on R4 phenyl ring is primarily carbonyl and amino-derived moieties as set forth in the working examples with 1

example of a cyano-guanidino derivative and another example of an aminosulfonyl. Some of the examples do not even appear to be claimed such as egs. 63,86,98 and 100. Thus the majority of R5 substituted derivatives which can be present up to 2 times on phenyl, naphthyl rings as well as additional substituents that can be present on piperazine carbons and benzyl ring have not been shown by adequate representation to possess minimum activity needed to practice the invention. There is no reasonable assurance as to what other substituents will work as there is no test data reported and even if it were in this case, the homogeneity of the species would provide no insight into structure-activity trends that need to be evaluated. Receptor binding is known to be structure-sensitive in general. Note In re Surrey 151 USPQ 724 regarding sufficiency of disclosure for a Markush group where as herein no examples of a diverse nature have been made much less tested showing the requisite activity needed to practice the invention. Also see MPEP 2164.03 for enablement requirements in cases directed to structure-sensitive arts such as the pharmaceutical art. Also note the criteria for enablement as set out in In re Wands cited in MPEP 2164.01(a), August 2000 edition, which includes factors such as:

- 1) Breadth of the claims- the claims cover compounds easily in the billions as pointed out above;

2) Level of unpredictability in the art- the invention is pharmaceutical in nature involving antagonistic activity at a particular receptor (CCR1). It is well established that “the scope of enablement varies inversely with the degree of unpredictability of the factors involved” and physiological activity is generally considered to be unpredictable. See *In re Fisher* 166 USPQ 18; Note Trivedi review article provided by the examiner on p.192, section entitled “CCR1 Receptor Antagonists”.

3) Direction or guidance- as stated above the compounds actually made are much closer to each other than to remaining scope ;

4) Working examples- No test data has been presented only description of testing protocols and thus no clear evaluation of which functional groups at various positions out of the many claimed might affect potency to a large or small degree.

In view of the above considerations, this rejection is being applied.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 10,11,20 and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bauman (US or WO provided by applicants). Bauman teaches for very similar compounds to that claimed herein treating uses such as antiinflammatory disorders based on binding to chemokine receptors as relied on herein. See columns 5,28 in US Bauman and pages 6 and 40 of WO'771. While compounds particularly described do not appear to anticipate the instant scope they are obvious variants since the sole difference is in the choice of substituent

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permitted on R3 ring of Bauman corresponding to instant R5. Species such as one listed on p.52, lines 26-27 (or the same in col.37, lines 28-30) differ only in having a carbonyl group present in the complex moiety present on the phenyl ring. Said moiety corresponds to alkoxycarbonylalkyl**carbonyl**aminoalkyl. However, alkoxycarbonylalkylaminoalkyl is also taught as a choice and as a preferred embodiment and this moiety is embraced in the instant claims. Thus it would have been obvious to one skilled in the art at the time the invention was made to replace the exemplified moiety pointed out above with that instantly claimed and in so doing obtain other compounds for antiinflammatory use in view of the teachings outlined above.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 10,11,20,25 and 26 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims of U.S.

Patent No. 6649611. Although the conflicting claims are not identical, they are not patentably distinct from each other because the species presented in tabular form in the US patent is also covered by the instant claims. Instant case is a continuation of US'611.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Emily Bernhardt whose telephone number is (571) 272-0664.

If attempts to reach the examiner by phone are unsuccessful, the supervisor for AU 1624, Dr. Mukund Shah, can be reached at (571)272-0674.

The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.



EMILY BERNHARDT

PRIMARY EXAMINER

Group 1600